REMARKS

With entry of this response, claims 1-50 are pending in the application.

Compliance of Information Disclosure Statement with 37 C.F.R. § 1.98(a)(1)

In reply to the Office Action dated December 18, 2001 (Paper No. 7), Applicant's Response dated March 18, 2002 included copies of the March 26, 2001 Information Disclosure Statement, Transmittal Form, Form PTO-1449, and return postcard. The Examiner had earlier stated in a telephone conversation with Applicant's representative, Ms. Felicity Groth, that he would allow Applicant's March 21, 2001 date for filing of the Information Disclosure Statement. Under 37 CFR § 1.98(d)(2), an Information Disclosure Statement was submitted in an earlier filed application, 09/481,058, filed January 11, 2000, the earlier-filed application is properly identified in the instant application and is relied on for an earlier effective filing date under 35 U.S.C. § 120. To fully comply with 37 C.F.R. § 1.98(a) through (c), Applicant encloses herein, copies of the March 26, 2001 Information Disclosure Statement, Transmittal Form, Form PTO-1449, return postcard and legible copies of each U.S. and foreign patent and each publication listed. Applicants respectfully request that the March 21, 2001 date for filing of the Information Disclosure Statement be entered.

Patentability Under 35 U.S.C. § 112

Claims 1-12 and 26-38 are rejected under 35 U.S.C. § 112, first paragraph, for alleged lack of enablement. Although the Office recognizes that the disclosure is enabling for the treatment of breast cancer, the Office asserts that the specification fails to provide enablement for the prevention or prophylaxis of breast cancer. Applicant respectfully traverses the rejection.

Applicant maintains that the specification enables the full scope of the claims by providing a method and composition for prophylaxis and treatment of breast cancer in a mammalian patient. As stated previously, evidence sufficient to determine that a disclosure satisfies the enablement requirement, including whether undue experimentation is necessary, requires consideration of several factors. *In re Wands* 8 USPQ 2d 1400, 1404 (Fed. Cir. 1988). The Office contends that methods and compositions for prophylaxis of breast cancer are inherently unpredictable. However, Applicant's disclosure provides detailed, *in vivo* animal

model assays for assessing operability of the invention that do not require undue experimentation. In this context, the Office has a burden of establishing sufficient factual evidence that is "inconsistent" with Applicants' assertions, and which *prima facie* demonstrates that the contested claims are not enabled. In re Marzocchi et al., 169 USPQ 367 (CCPA 1971). Any such evidence that is not supported by documentation but is founded within the Examiner's personal knowledge must be articulated in the appropriate context and form, in compliance with 37 C.F.R. § 1.107(b) and MPEP 707.05.

Since the initial burden is on the examiner to give reasons for the lack of enablement, the examiner must also give reasons for a conclusion of noneablement that is inconsistent with Applicant's disclosure. In this context, a rigorous or an invariable exact correlation is not required, "where the disclosure of pharmacological activity is reasonable based upon the probative evidence." *Cross v. Iizuka*, 224 USPQ 739, 747 (Fed. Cir. 1985). In the instant case, the disclosure teaches that DMBA-induced mammary carcinoma in rats can be prevented or inhibited by nasal administration of carbetocin. The specification further teaches that mammary carcinoma will be inhibited or prevented in SCID mice engrafted with human mammary carcinoma cells (MCF7 or MDA-MB231 cells).

Applicant respectfully submits that the Office has not met its initial burden to provide sufficient factual basis to demonstrate nonenablement of the pending claims. The mere fact that cancer prevention may be unpredictable does not establish, a priori, that all claims to such methods are impracticable. Nor is it required to demonstrate that an enabling method or composition for prophylaxis of tumor initiation or growth is effective in all cases, or is optimally effective in a particular application. Accordingly, Applicant respectfully requests that the rejection of claims 1-12 and 26-38 under 35 U.S.C. § 112, first paragraph be withdrawn, or that clarification of the grounds for rejection be provided by the Office.

Patentability Under 35 U.S.C. § 112

Applicant acknowledges that the Office has reconsidered and withdrawn the rejections set forth in the prior Office Action dated December 18, 2001 (Paper No. 2) under 35 U.S.C. § 102.

Patentability Under 35 U.S.C. § 103

Claims 1-12, 26-33 and 39-50 stand rejected under 35 U.S.C. § 103(a) as allegedly unpatentable over U.S. Patent 5,482,931 to Harris et al. (Harris et al.) in view of Cassoni et al. (*Virchows Archive* **425**: 467-472, 1994). Applicant respectively traverses the rejection and submits that the subject matter of claims 1-12, 26-33 and 39-50 is neither disclosed nor suggested by the collective teachings of the Harris et al. and Cassoni et al. references.

Harris et al. is cited for allegedly teaching "pharmaceutical compositions of peptides, inter alia oxytocin and their analogues and derivatives," including carbetocin. The Office relies on Cassoni for allegedly teaching "the administration of oxytocin or with an analogue of oxytocin to inhibit breast cancer growth." The Office further asserts that one having ordinary skill in the art at the time of the invention would have been motivated to utilize the preferred pharmaceutical peptide of carbetocin as a treatment of breast cancer because carbetocin is an analogue of oxytocin.

To establish a *prima facie* case of obviousness, three requirements must be satisfied: first there must be some suggestion or motivation to modify the reference or to combine the reference teachings; second, there must be a reasonable expectation of success for achieving the claimed invention and its particular results; and, third, the prior art references must teach or suggest all the claim limitations. See *In re Vaeck*, 20 U.S.P.Q. 2d 1438 (Fed. Cir. 1991). The requisite "reasonable expectation of success" must be founded in the prior art, not in the applicant's disclosure.

In the instant case, Cassoni et al. reports that no significant effect of oxytocin on the proliferation rate of MCF7 cells was observed. *See* Figure 1D of Cassoni et al., page 468. Cassoni et al. notes previous reports that underscore the uncertainty regarding possible effects of oxytocin on breast cell growth, differentiation, and survival. Specifically, Cassoni et al. emphasizes (at page 471, paragraph bridging columns 1 and 2) that Taylor et al. (*Cancer Res.* **50**:7882-7886, 1990) found a significant *enhancement* of the growth rate of MCF7 cells as a result of oxytocin administration at low concentrations in the range of 10^{-9} to 10^{-12} M. In considering these teachings, Applicant notes that each prior art reference relied upon by the Office must be considered in its entirety, including disclosures that would teach away from the

claimed invention. *See W.L. Gore & Associates, Inc. v. Garlock, Inc.*, 220 U.S.P.Q. 303 (Fed. Cir. 1983), *cert. denied*, 469 U.S. 851 (1984).

Based on these and other teachings (as noted in the application at page 4, lines 5-24), conflicting reports at the time of the present invention gave rise to substantial uncertainty regarding the potential utility of oxytocin, oxytocin analogues, and other hormonal factors as therapeutic agents for successful prophylaxis and treatment of breast cancer. Because the complex roles of these diverse agents remained undefined, the record fails to establish a reasonable expectation of success to practice the instantly claimed invention to obtain the particular results described by Applicant. Accordingly, it is respectfully urged that the rejection of claims 1-12, 26-33 and 39-50 under 35 U.S.C. §103(a) over Harris et al. in view of Cassoni et al. be withdrawn.

Claims 13-25 and 34-38 stand rejected under 35 U.S.C. § 103(a) as allegedly unpatentable over U.S. Patent 5,482,931 to Harris et al. (Harris et al.) in view of Boer et al. (*Peptides* **13**: 1083-1085, 1992). The Office further cites Leckman et al. (*Psychoneuroendocrinology* **19**: 723-749, 1994) for allegedly teaching administration of oxytocin for treating obsessive-compulsive disorder. Applicant respectfully traverses the rejection under 35 U.S.C. § 103 and submits that the subject matter of claims 13-25 and 34-38 is neither disclosed nor suggested by the collective teachings of the Harris et al., Boer et al., and Leckman et al. references.

Harris et al. is cited for allegedly teaching pharmaceutical compositions of peptides, inter alia oxytocin and their analogues and derivatives, including carbetocin. Leckman et al. is cited for allegedly teaching administration of oxytocin to treat obsessive-compulsive disorder. The Office argues that "the skilled artisan would have been motivated to employ the oxytocin and its analogues and derivatives, including carbetocin, to treat the diseases and abnormal conditions of the psychiatric disorder of obsessive compulsive disorder."

Applicant respectfully submits that the cited references fail to teach or suggest administration of an oxytocin analogue to successfully alleviate an obsessive-compulsive behavior in a mammalian subject. Both Boer et al. and Leckman et al. specifically teach away from the instantly claimed subject matter. In particular, Boer and colleagues state that they:

> observed no reduction in the number of compulsive behaviors, ... neither in the oxytocin group, nor in the placebo group. The present results indicate that oxytocin at the dosage used in this study, does not possess anticompulsive properties. In addition, no significant reductions in the associated anxious and depressive symptomatology were observed. (underscore added).

On this basis Boer and coworkers concluded that at two different dosages administered to patients, they observed no anticompulsive properties of oxytocin. See Boer et al., page 1085, paragraph bridging columns 1 and 2. Similarly, Leckman et al. teach away from Applicant's claimed invention by concluding that " a role for oxytocin in the pathogenesis of obsessive compulsive disorder is meager and has mostly focused on systemically administered oxytocin's equivocal value as a therapeutic agent." Leckman et al. state further that oxytocin delivered systemically via intravenous, intraperitoneal or intranasal routes is an ineffective therapy. See Leckman et al., page 727, 1st paragraph. Harris et al. is limited to a generalized teaching of "stabilized aqueous pharmaceutical compositions" of small and medium-size peptides. The reference focuses on a distinct pharmacological agent desmopressin, and only incidentally mentions carbetocin. The Office states that Harris et al. "specifically teach the use of oxytocin and its derivatives and analogs, which includes carbetocin, to treat diseases and abnormal conditions." It is clear, however, that Harris is not directed to any specific disease or abnormal condition contemplated for treatment within the instant invention. On the contrary, to rely on this reference for teaching a specific therapeutic application of carbetocin or any other oxytocin analogue is entirely unfounded. To substantiate this position, the Office would have to demonstrate that a person of ordinary skill in the art would interpret the teachings of Harris et al. as a convincing report that carbetocin (along with a host of other, unrelated compounds identified in the reference) is effective for treating all "diseases and abnormal conditions"—particularly including breast cancer and specific psychiatric disorders to which the instant invention is directed. The record clearly fails to support such a conclusion.

In view of the foregoing, Applicant respectfully submits that the proposed combination of Harris et al. in view of Boer et al. and further in view of Leckman et al. does not teach or suggest, but rather specifically teaches away from Applicant's claimed invention. Accordingly,

it is respectfully urged that the rejection of claims 13-25 and 34-38 under 35 U.S.C. §103(a) be withdrawn.

Claims 26-37 stand rejected under 35 U.S.C. § 103(a) as allegedly unpatentable over U.S. Patent 5,482,931 to Harris et al. (Harris et al.). Applicant respectfully traverses the rejection under 35 U.S.C. § 103 and submits that the subject matter of claims 26-37 is neither disclosed nor suggested by the teachings of Harris et al.

The Office again cites Harris for teaching "pharmaceutical compositions of peptides, namely carbetocin, ... for management of diseases and abnormal conditions." As noted above, Harris et al. clearly fail to teach or suggest the efficacy of carbetocin or another oxytocin analog for prophylaxis or treatment of breast cancer or a psychiatric disorder in a mammalian patient. The assertion of authority (Sinclair v. Interchemical Corp.) regarding "selection of a known material based on its suitability for its intended use" is therefore clearly inapposite to the instant case. Harris clearly does not teach the suitability of carbetocin or any other oxytocin analogues for the instantly claimed uses. Applicant further notes that the defective teachings of Harris et al. are underscored by the Cassoni et al., Boer et al., and Leckman et al. references that clearly teach away from using the claimed composition for prophylaxis and treatment of breast cancer or a psychiatric disorder, as noted above. Accordingly, it is respectfully urged that the rejection of claims 26-37 under 35 U.S.C. §103(a) over Harris et al. be withdrawn.

Claims 11, 12, 32, 49 and 50 stand rejected under 35 U.S.C. § 103(a) as allegedly unpatentable over U.S. Patent 5,482,931 to Harris et al. (Harris et al.) in view of Cassoni et al. (*Virchows Archive* **425**:467-472, 1994) and further in view of Lipton et al. (*J. Endocrinology* **103**: 383-388, 1984). Applicant respectfully traverses the rejection under 35 U.S.C. § 103(a) and submit that the subject matter of claims 11, 12, 32, 49 and 50 is neither disclosed nor suggested by the collective teachings of the Harris et al., Cassoni et al., and Lipton et al. references.

As stated above, Harris et al. is cited for allegedly teaching "pharmaceutical compositions of peptides, inter alia oxytocin and their analogs and derivatives," including carbetocin, and Cassoni et al. is cited for allegedly teaching "the administration of oxytocin or with an analog of oxytocin to inhibit breast cancer growth." The Office further cites Lipton et al. for allegedly teaching "the administration of tamoxifen or oestradiol to treat breast cancer." The Office asserts that "it is prima facie obvious to combine two compositions each of which is taught by

the prior art to be useful for the same purpose, in order to form a third composition to be used for the very same purpose. ... [T]he idea of combining them flows logically from their having been individually taught in the prior art." *In re Kerkhoven*, 205 USPQ 1069, 1072 (CCPA 1980).

Applicant respectfully submits that a prior art reference must be considered in its entirety, including disclosures that would teach away from the claimed invention. See *W.L. Gore & Associates, Inc. v. Garlock, Inc.*, 220 U.S.P.Q. 303 (Fed. Cir. 1983), *cert. denied*, 469 U.S. 851 (1984). In the instant case, Lipton teaches that the administration of tamoxifen or oestradiol-17ß *inhibits* responses stimulated by oxytocin. See Figure 1 of Lipton, page 385; Figure 4 of Lipton, page 386. Thus, Lipton teaches directly away from the proposed combination based on Harris et al. and Cassoni et al. to achieve a combined effect of estradiol or tamoxifen with oxytocin on breast cancer cell growth. Accordingly, one having ordinary skill in the art would not be motivated to combine the teachings of Lipton et al. with those of Harris et al. and Cassoni et al. to achieve a combinatorial effect in the prophylaxis or treatment of breast cancer. Accordingly, it is respectfully urged that the rejection of claims 11, 12, 32, 49 and 50 under 35 U.S.C. §103(a) over Harris et al., in view of Cassoni et al. and Lipton et al. be withdrawn.

CONCLUSION

In view of the foregoing, Applicant respectfully submits that all claims now pending in this Application are in condition for allowance. The issuance of a formal Notice of Allowance at an early date is therefore earnestly solicited.

If the Examiner believes that a telephone conference would expedite prosecution of this application, please telephone the undersigned at 206-332-1380.

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Respectfully submitted,

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